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Natural fiber reinforced biodegradable staples: Novel approach for efficient wound closure

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ABSTRACT

Every year millions of lacerations and incisions taken place and require an effective methodology to manage the wound for a better life. The primary causes include mechanical trauma and surgical procedures. The rapid healing of the wound is critical to prevent further infection and reduction pain etc. Current options comprise of sutures, staplers, surgical strips and glues, again the intervention depends on the type of wound and the surgeon preference. The current wound closure techniques pose various potent limitations and confronting the problems to create a desired wound closure technique is necessary for faster and effective wound healing management. The surgical staplers are fast and easy to use wound closure devices, which approximates the edges of the wounds together by staples. The staples are mostly made up of metals like titanium and stainless steel. By modifying the existing stapling method using biodegradable staples that are expected to have good mechanical properties, not require removal procedure, minimized scarring and an overall acceleration in wound healing with minimal complications. Present, the paper focuses on the novel hypothesis on natural fiber reinforced biodegradable polymer staples as wound enclosures with high strength and degradability.

Introduction

Surgical incisions and traumatic injuries are considered as external injuries which further progress to acute wounds by physical alterations of cells [1]. The wounds healed through a timely and orderly repairing process. Over 100 million surgical procedures performed each year worldwide. Among these, around 50 million wounds traumatic in nature and 80% wounds require some kind of enclosure procedure [2]. The wound healing process is a dynamic and complex, involves a series of sequential process, starts with hemostasis, inflammation, proliferation and ends with tissue remodeling (Fig. 1).

In order to prevent the wound associated complications and infections, proper wound management is indispensable [3]. Immediately after injury, the haemostatic phase starts by a sequence of events such as bleeding, vasoconstriction activation of platelet and initiation of the inflammatory response [4]. Followed by the inflammatory phase, which conspires the activation of macrophages and migration of cytokine and growth factor, results in the initiation of angiogenesis [5]. Simultaneously, wound debris and bacteria are eliminated by neutrophils. Subsequently, the proliferation phase begins with the migration of fibroblasts and endothelial cells to the wound site. Then, the fibroblasts synthesize the collagen and converted into myofibroblast for contraction of the wound. The wound heals by the remodeling phase (final) where collagen is remodeled from type III to type I [6]. At wound site, the fibroblasts form a new provisional extracellular matrix (ECM) by the secretion of collagen and fibronectin [7]. Concurrently, the re-epithelialization of the epidermis occurs, in which epithelial cells proliferate and deposit on top of the wound bed, providing cover for the new tissue [8].

Generally, chronic wounds fail to heal in an orderly manner, due to the conditions such as complex diseases (diabetes and high blood pressure), infection, smoking, age, and other factors hamper the appropriate wound healing mechanism [9].

Though the natural mechanism initiates the healing process of the injury, but unable to manage the complete healing. Auxiliary external wound closure practice is necessary for efficient wound healing management. Primarily, surgical sutures (biodegradable and non-biodegradable) glues, strips and staples are the well known interventions. Basically, the wound healing management has two intention, primary intention is to join the edges together by auxiliary enclosure technique to promote faster wound healing. A secondary intention is to promote the healing without enclosure mechanism cases such as burns, ulcer

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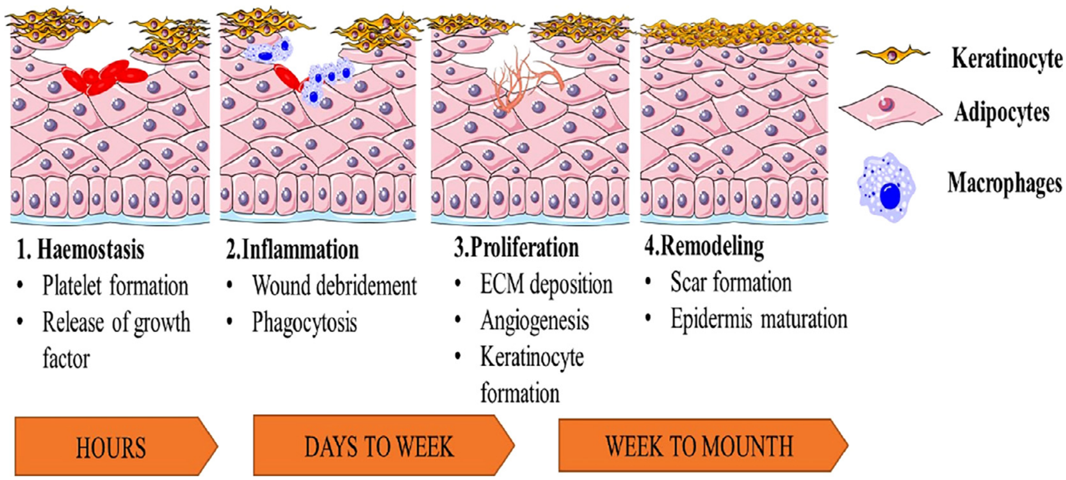

Fig. 1. The illustration represents the physiological mechanism of wound healing mechanism.

wounds and the contaminated area where wound enclosure is unable to practice. These type of wounds took a significantly longer time to heal than primary intention healing [9].

Wound closure techniques

The art of wound management has been developed with huge demand and still exploring for better techniques. The most commonly used techniques are sutures, staples, adhesive tapes and glues as shown in Fig. 2. Sutures and staples are the invasive types of closure used for long incisions, and areas of high tension. While adhesive strips and glues are the non-invasive types of closure, which is simple to use, and used for simple lacerations to support after removal of surgical staples and suture. The advantages of these methods include less pain, minimal scarring, and minimal skin reaction [10].

The selection of the closure material widely depend upon the surgeon preference, and other factors like location, wound type, age, cost-effectiveness and other considerations. However, there is no ideal technique to serve all complications. Therefore, there is a high need to develop a closure technique with cost-effectiveness, patient-friendly, less painful and on site antibiotic delivery [11].

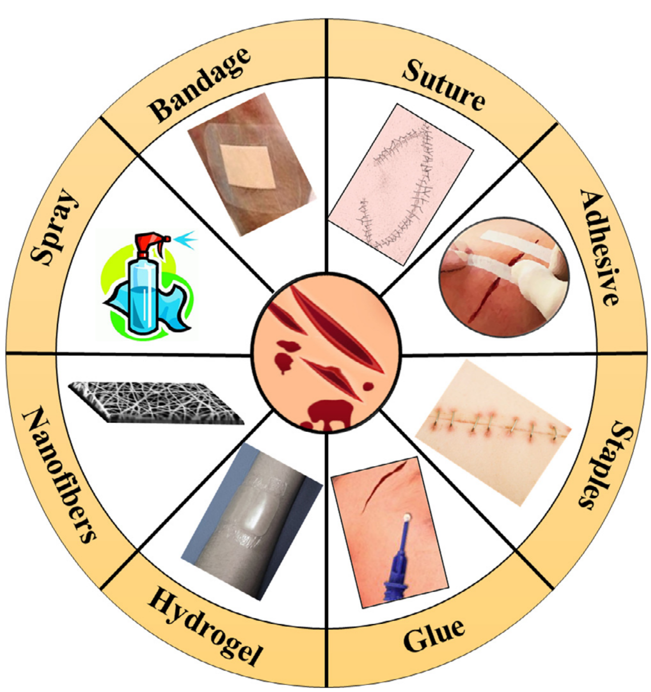

Fig. 2. The illustration showing various approaches for wound management and healing.

Current strategies for wound closures

Suturing is the oldest and most commonly used closure technique. It comprises a metal needle where the thread is attached and the process is similar to conventional sewing. There are different types of sutures which can be broadly classified into biodegradable and non-biodegradable [11]. The absorbable sutures are fabricated from catgut, polyglycolic acid and polyglactin while non-absorbable sutures prepared from nylon, polypropylene, silk etc. Most recently, the antibacterial coated sutures like Vicryl Plus is commercially available and it shows strong resistance to bacterial colonization thereby prevents the surgical site infection [12]. Besides, sutures adhesive strips and glues are known for non-invasive wound enclosures and widely used for small cuts. The adhesive strips widely used for superficial wounds while strips applied across the laceration wound to approximate the edges together [13]. Furthermore, the octylcyanoacrylate glues also commonly used for simple traumatic lacerations. Where the cyanoacrylate polymerizes and transforms into a protective film in contact with tissue thereby and holds the wound edges together. The glues are known for rapid enclosing with antimicrobial activity [14,15]. The polymeric hydrogels are emerging as potential materials for wound management and repair in recent days. The easy alteration of chemical and physical properties of hydrogels made them strong wound closure materials for various kinds of tissues. The practice of hydrogels is quite easy as compared to other techniques and provides sufficient mechanical strength to hold the edges of the wound. Further, the hydrogel act as a barrier to bacterial infection absorbs wound exudates and keep the wound moist for fast healing [16]. The vacuum-assisted closure therapy is used to manage complex traumatic wounds. The technique uses topical negative pressure to remove the blood and other fluids at the site of the wound to counter the infection. The procedure promotes increased localised blood flow, thereby enhancing the supply of oxygen and nutrition to the wound which leads to accelerated healing [17]. Bandages are the most frequently used wound management technique as a first aid option. The combination of antibiotics and other drugs with bandages resist infection and inflammation to further progression of the wound for further therapy in complex injuries [18]. Most recently introduced stapler technology gains much interest as wound closure. The handling of surgical staplers are easy, requires less expertise, and time-saving in an emergency. Most significantly, the staples are preferred for scalp wounds under tension, traumatic linear injuries and all kind of surgeries [11]. Besides, staplers are less prone to infection than surgical sutures [19]. Like sutures, staples are classified into absorbable and non-absorbable. The non-absorbable staples are mostly made up of metals like stainless steel and titanium which have excellent mechanical strength. But the problem with these staples is that these staples need to be removed after some time which causes a significant amount of discomfort and extra cost to the patient. The biodegradable form of staple material that is available in the market is made up of PLGA copolymer has been reported [11,20].

Disadvantages of current wound closure techniques

Suturing requires expertise particular in nonlinear wounds and the outcome widely depends on the skill level of the surgeon. Although the sutures are sterilized but it has a high risk of infection by space offering for bacterial colonies in braided of sutures [21,22]. Besides, the duration of suturing is also longer as compared to other wound enclosing techniques [11,13]. Whereas adhesive strips are unable to bind adequately in wet areas, areas under tension and holds lowest tensile strength among all the wound closure techniques. Strips are basically recommended for small lacerations, as a reinforcement for surgical staples and sutures [11,13]. The adhesive strips practiced for linear wounds rather than for irregular injuries or wounds [10]. The major limitations for cyanoacrylate glues are the high cost, burning effect by local polymerization, fatigue failure of cured glue and limit to apply on high tension areas due to its low mechanical strength [23]. Surgical metal staples provide adequate mechanical strength to hold the edges of the wound but the post healing removal is necessary and causes pain and sometimes inflammation. Moreover, metal staples are difficult to use in lacerations [11,24]. Therefore, each wound closure technique comes with its own disadvantages and there is no ideal enclosure system for all kind of wounds. Hence, there is an urgent need to develop a new technology or the improvement of existing practices for a better wound closure system.

Need for biodegradable staplers

Staples are quite easy to use, primarily where the sophisticated medical facility is not available and it requires minimal expertise unlike sutures [11]. Moreover, the risk of surgical site infection is less and gives good cosmetic results [25]. The concept of biodegradable staples is to avoid the painful removal of staples after healing generally seen in metallic staples. More significantly, the degradable staples most useful for internal tissue wound enclosure and veterinary where it is difficult to bring back the animal for removal of wound enclosure. The development and fabrication of biodegradable staples with good mechanical strength is very essential to fulfilling the objective.

Hypothesis

The closing of wound or injury edges together is known to enhance the healing and repair of the wound. Generally, techniques such as suturing, stapling and glues etc. are widely practiced, however, there is no ideal technique to address the objective. Therefore, there a space to develop novel materials and strategies to fill the gap. The proposed hypothesis give the strategy to develop a novel composite material with higher mechanical strength with optimum degradation time. The polymer based nanocomposite will be able to withstand the tension at the wound site and able to use all kind of wounds due to its low stiffness. The hypothesis is carried out by the development of nanocomposite with high strength and degradable polymer (PLLA) reinforced with suitable degradable nanofibers (Cellulose acetate) (Fig. 3). Due to the reinforcement material, the composite will get enhanced mechanically and modulated the degradation time.

The developed degradable staples may have huge market potential since there is no such established product is available for wound enclosing. Furthermore, the staples can be coated with a suitable antibiotic for onsite delivery to prevent surgical infections.

Evaluation of hypothesis

The current practice of wound enclosers is depended on various factors such as the decision of physician, type of wound, cost-effectiveness and patient compliance etc. However, the current practices have their limitations to counter contemporary changes. The proposed hypothesis of degradable staples may answer the maximum hurdles in wound enclosure.

Fabrication of biodegradable staples

The staples are manufactured in different methods and it depends on the material. The metal staples are mostly manufactured by cold drawing method, where the metal wire is pulled through a die without preheating [26]. As the metal is drawn, it stretches thinner into a desired shape and thickness. The average diameter of metal surgical staples is around 0.5 mm with length and breadth at around 5 mm and 3.5 mm, respectively [27]. The low strength polymeric staples fabricated by techniques like extrusion, injection molding and compression molding etc. The injection molding is a common method to fabricate various shapes of the polymer. Where the melted polymer injected into a tightly packed mould and cooled it to make the desired shape [28]. While in compression moulding the material is usually heated to make polymer softer, placed in the desired mould and pressed with high pressure to make a uniform shape [29]. The proposed hypothesis is utilized anyone the techniques to fabricate the staples by utilizing appropriate mould.

Materials for fabrication of biodegradable staples

Various biodegradable polymers have been employing for fabrication bioabsorbable sutures commercially such as Polygalactic acid (PGA), polydioxanone (PDS), polylactic acid (PLA), poly (lactic-co-glycolic) acid (PLGA), etc. [30]. However, the staples need higher mechanical strength and Young's modulus as compared to the surgical sutures. In contrast to this poly-L-lactic acid (PLLA) is the right choice for the present hypothesis.

Properties of poly-L-lactic acid (PLLA)

PLLA is FDA approved biodegradable polymer with well mechanical properties [31]. Basically, the polylactic acid exists in two forms of isomer i.e. poly (L-lactic acid) and poly (D-lactic acid) (PDLA) as shown in Fig. 4 [32]. PLA has a high tensile strength (15.5–150 MPa) and high thermal stability (melting point 170–200°) [33]. PLLA is the lower crystalline form and it has been used for various biomedical applications such as implant materials, sutures and drug delivery due to its good biocompatibility and biodegradability. Although the PLLA has good mechanical strength, but its brittleness limits its application for high tension applications to hold the stress for longer time intervals [34–38]. The polymer is soluble in organic solvents like benzene, chloroform, and acetonitrile etc. The glass transition temperature (T_g) of PLLA is around 55–60 °C, melting temperature (Tm) is ~180 °C and its half-life in 37 °C normal saline is around 4–6 months but its degradation highly depends on its molecular weight, pH of the environment [39]. Therefore the polymer is highly suitable for biomedical applications, while it needs modifications to use for high strength applications.

Reinforcement of polymer using natural fibers

Generally, the polymers exhibit significantly lower mechanical strength as compared to metal counterparts. Therefore, the modification of the polymer is required to enhance the mechanical strength to fabricate surgical staples. The fiber reinforcement is one of the best

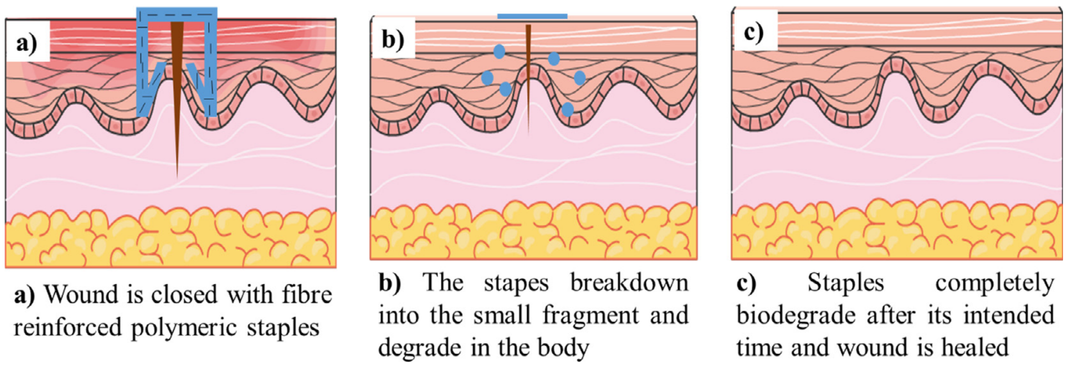

Fig. 3. The illustration presents the strategy of the biodegradable stapled wound, where the wound is closed with the staple subsequently wound is healed with simultaneous degradation of the staple.

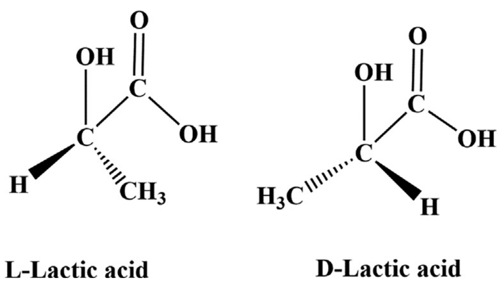

Fig. 4. The chemical structure of stereoisomer's of Lactic acid.

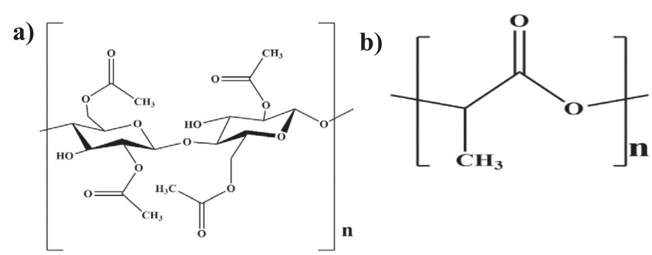

Fig. 5. The chemical Structures of (a) cellulose acetate and (b) PLLA.

methods to enhance the mechanical strength of the material. The fibers like glass, steel, polymer and some naturally derived fibres are widely used to reinforce the matrix material to enhance the mechanical and physical properties [40]. The fiber improves the flexural-tensile strength as well as gives impact resistance and improve toughness. Fiber reinforced composites are widely used in engineering industry like locomotive parts, aircraft and many other areas in which mechanical strength is essential attributes [41]. The natural fibres are generally preferred for medical applications due to their biocompatibility and degradation. The use of natural fiber reinforcement was reported for orthopedic implants for the improvement of mechanical strength [42]. Moreover, the natural fibers are abundantly present in plants and consist mainly of cellulose, hemicelluloses, lignin and pectin and the common plants from where they are taken are cotton, sisal, hemp, bamboo and jute etc. [43]. The natural fibers themselves are not suitable to be used to sustain the range of loads expected in many biological applications but as a reinforcing agent, they indeed enhance the properties of matrix material [44]. The natural fiber reinforced PLLA composites are reported for various applications [45–55]. There are several factors to be considered before choosing appropriate natural fiber for use in biomedical applications such as biocompatibility, biodegradability, sterilizability, manufacturability and mechanical properties [56]. However, the properties of natural fibers vary between the plant species, cultivation and processing methods [57]. Therefore, to avoid the variable properties, the purified form of fibre is the best choice to use as reinforcing material. The fibers reinforced PLLA composites can be prepared by methods like extrusion, compression and injection molding [58,59]. The successful fabrication of high strength staples is highly depended on the optimization of the fiber concentration for PLLA composite [50,60]. The cellulose acetate nanofiber is a potential candidate to enhance the mechanical properties surgical staples of PLLA.

Cellulose acetate

Cellulose acetate is the acetate ester of natural cellulose which is produced by reacting cellulose with acetic acid and acetic anhydride - with the presence of sulphuric acid [61]. Its structure is shown in Fig. 5. The number of acetylation determines its hydrophobic or hydrophilic property and this can be tuned according to its potential application [62].

The hydrophobic cellulose acetate is considered to be a better candidate as filler for hydrophobic PLLA since the cellulose acetate promotes the strong hydrophobic bond with the polymer matrix to increase the physicochemical properties of the composite [63]. The degree of hydrophobicity is controlled by the presence of acetate and more the acetate, higher the hydrophobicity [64]. The naturally abounded cellulose acetate is known for better biocompatibility, biodegradability and significantly high mechanical properties. The tensile strength, Young's modulus and elongation at break around of cellulose acetate are 55 MPa, 4.5 GPa, and 25–30%, respectively [65]. The cellulose acetate has been widely used for filter material in dialysis and in wound dressings [66]. It is desirable to have a uniform size of cellulose acetate fibres to get homogeneous dispersion in matrix and electrospinning technique is the best known for the fabrication of fibers [67]. Therefore the high strength, biocompatible and degradable cellulose acetate is the best choice for the present hypothesis.

Mechanism

Reinforced composites are known for advanced properties for various applications. The composites have been employed for various biomedical applications like the artificial jaw, joint sockets and bone cement etc. Among, fiber reinforced composites are better known for enhanced mechanical properties by its structural features. The materials like montmorillonite, hydroxyapatite, carbon and titanium fibers etc. are well known reinforcing materials for medical applications [68–74]. The mechanical properties such as ultimate tensile strength, stiffness, and fatigue life primarily rule the fate of material against functional stress of tissues. Indeed the fiber reinforced composites provide enhanced mechanical properties and but the distribution of fibers in polymer matric is highly impacted the mechanical properties by homogeneous stress distribution to resist the crack initiation [75]. The reported study suggested that the cellulose nanofibers reinforced (5%) PLA composite has shown 24% and 21% enhancement in modulus and tensile strength, respectively compared to plain PLA [76]. The literature suggests that the properties the composite are further enhanced by using aligned fibers and homogeneous dispersion of unaligned nanofibers in the PLA matrix [77,78]. The procedure of wound enclosing is similar to the metal staples. The moulded rigid composite staple is inserted into skin or tissue to hold the edges of the wound by using a suitable stapler. The increased in stiffness of fiber reinforced composite staples able to puncture the tissue and hold its shape for a longer time. The increased tensile strength prevent the mechanical failure of the staple at high tension areas of the wound. Therefore the enhanced mechanical properties will make the composite very reliable for use as a surgical staple material to close incisional and traumatic wounds. Subsequently, the staples will degrade to avoid secondary intervention to removal as in metallic staples.

Perspective

The proposed strategy of degradable staples for wound enclosure has potential advantages over the conventional strategies. Primarily, due to its biodegradability which will make it patient-friendly, require less expertise and economic. Moreover, there are numerous cost-effective techniques for staple development like extrusion, injection molding, compression molding etc. which are already established for fabrication of various shapes of polymer and composites. However, the critical part of the methodology is the fabrication of the composite by the optimization of the fiber content to get the desired mechanical strength. The fabrication technique will have an impact on its mechanical properties so the various parameters should be optimized for getting a high-quality product. Furthermore, fabricated staples can be coated with antibiotics to combat surgical site infections. The high mechanical strength and biodegradable property of composite can show a huge impact on wound closure market.

Conflict of interest

The authors declared that there is no conflict of interest.

Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.mehy.2019.03.021.

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